JU., 1 1 1000 HE WITTED STATES PATEN	Attorney Docket No. 01107.00098 PATENT T AND TRADEMARK OFFICE
In re Application of	)
Nicholas NICOLAIDES et al.	)

For: METHODS FOR GENERATING HYPERMUTABLE MICROBES

# SUBMISSION OF SEQUENCE LISTING

Assistant Commissioner of Patents & Trademarks Washington, D.C. 20231

Dear Sir:

Serial No. 09/780,675 Filed: February 12, 2001

A paper copy and a CRF of a sequence listing are submitted herewith to place the application in compliance with U.S. regulations. I believe that the sequences in the two forms of the sequence listing are identical and add no new matter to the application.

Respectfully submitted,

Date: June 11, 2001

Sarah A. Kagan Reg. No. 32,141

BANNER & WITCOFF, LTD. 1001 G Street, N.W. – Eleventh Floor Washington, D.C. 20001-4597 Telephone: 202/508-9100





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650

645

Ala Glu Asp Glu Leu Arg Lys Glu Ile Ser Lys Ser Met Phe Ala Glu 665 Met Glu Ile Leu Gly Gln Phe Asn Leu Gly Phe Ile Val Thr Lys Leu 680 Lys Glu Asp Leu Phe Leu Val Asp Gln His Ala Ala Asp Glu Lys Tyr 695 700 Asn Phe Glu Met Leu Gln Gln His Thr Val Leu Gln Ala Gln Arg Leu 710 715 Ile Thr Pro Gln Thr Leu Asn Leu Thr Ala Val Asn Glu Ala Val Leu 725 730 Ile Glu Asn Leu Glu Ile Phe Arg Lys Asn Gly Phe Asp Phe Val Ile 745 740 Asp Glu Asp Ala Pro Val Thr Glu Arg Ala Lys Leu Ile Ser Leu Pro 765 760 Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Ile Asp Glu Leu Ile 775 780 Phe Met Leu Ser Asp Ser Pro Gly Val Met Cys Arg Pro Ser Arg Val 790 795 Arg Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val Met Ile Gly 810 805 815 Thr Ala Leu Asn Ala Ser Glu Met Lys Lys Leu Ile Thr His Met Gly 830 825 Glu Met Asp His Pro Trp Asn Cys Pro His Gly Arg Pro Thr Met Arg 835 840 845 His Val Ala Asn Leu Asp Val Ile Ser Gln Asn 855

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<212> PRT <213> Homo sapiens

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Met Lys Gln Leu Pro Ala Ala Thr Val Arg Leu Leu Ser Ser Ser Gln 10 Ile Ile Thr Ser Val Val Ser Val Val Lys Glu Leu Ile Glu Asn Ser 25 20 Leu Asp Ala Gly Ala Thr Ser Val Asp Val Lys Leu Glu Asn Tyr Gly 35 40 45 Phe Asp Lys Ile Glu Val Arg Asp Asn Gly Glu Gly Ile Lys Ala Val 55 Asp Ala Pro Val Met Ala Met Lys Tyr Tyr Thr Ser Lys Ile Asn Ser 70 75 His Glu Asp Leu Glu Asn Leu Thr Thr Tyr Gly Phe Arg Gly Glu Ala 90 85 Leu Gly Ser Ile Cys Cys Ile Ala Glu Val Leu Ile Thr Thr Arg Thr 105 Ala Ala Asp Asn Phe Ser Thr Gln Tyr Val Leu Asp Gly Ser Gly His 120 125 Ile Leu Ser Gln Lys Pro Ser His Leu Gly Gln Gly Thr Thr Val Thr 130 135 Ala Leu Arg Leu Phe Lys Asn Leu Pro Val Arg Lys Gln Phe Tyr Ser 150 155 Thr Ala Lys Lys Cys Lys Asp Glu Ile Lys Lys Ile Gln Asp Leu Leu 165 170 Met Ser Phe Gly Ile Leu Lys Pro Asp Leu Arg Ile Val Phe Val His 185 Asn Lys Ala Val Ile Trp Gln Lys Ser Arg Val Ser Asp His Lys Met 200 205

Ala Leu Met Ser Val Leu Gly Thr Ala Val Met Asn Asn Met Glu Ser 215 Phe Gln Tyr His Ser Glu Glu Ser Gln Ile Tyr Leu Ser Gly Phe Leu 230 235 Pro Lys Cys Asp Ala Asp His Ser Phe Thr Ser Leu Ser Thr Pro Glu 245 250 Arg Ser Phe Ile Phe Ile Asn Ser Arg Pro Val His Gln Lys Asp Ile 260 265 Leu Lys Leu Ile Arg His His Tyr Asn Leu Lys Cys Leu Lys Glu Ser 280 285 Thr Arg Leu Tyr Pro Val Phe Phe Leu Lys Ile Asp Val Pro Thr Ala 300 295 Asp Val Asp Val Asn Leu Thr Pro Asp Lys Ser Gln Val Leu Leu Gln 310 315 Asn Lys Glu Ser Val Leu Ile Ala Leu Glu Asn Leu Met Thr Thr Cys 325 330 335 Tyr Gly Pro Leu Pro Ser Thr Asn Ser Tyr Glu Asn Asn Lys Thr Asp 345 350 340 Val Ser Ala Ala Asp Ile Val Leu Ser Lys Thr Ala Glu Thr Asp Val 365 360 Leu Phe Asn Lys Val Glu Ser Ser Gly Lys Asn Tyr Ser Asn Val Asp 375 380 Thr Ser Val Ile Pro Phe Gln Asn Asp Met His Asn Asp Glu Ser Gly 390 395 Lys Asn Thr Asp Asp Cys Leu Asn His Gln Ile Ser Ile Gly Asp Phe 405 410 Gly Tyr Gly His Cys Ser Ser Glu Ile Ser Asn Ile Asp Lys Asn Thr 420 425 430 Lys Asn Ala Phe Gln Asp Ile Ser Met Ser Asn Val Ser Trp Glu Asn 435 440 445 Ser Gln Thr Glu Tyr Ser Lys Thr Cys Phe Ile Ser Ser Val Lys His 455 460 Thr Gln Ser Glu Asn Gly Asn Lys Asp His Ile Asp Glu Ser Gly Glu 470 475 Asn Glu Glu Glu Ala Gly Leu Glu Asn Ser Ser Glu Ile Ser Ala Asp 485 490 Glu Trp Ser Arg Gly Asn Ile Leu Lys Asn Ser Val Gly Glu Asn Ile 500 505 Glu Pro Val Lys Ile Leu Val Pro Glu Lys Ser Leu Pro Cys Lys Val 515 520 525 Ser Asn Asn Asn Tyr Pro Ile Pro Glu Gln Met Asn Leu Asn Glu Asp 540 530 535 Ser Cys Asn Lys Lys Ser Asn Val Ile Asp Asn Lys Ser Gly Lys Val 555 550 Thr Ala Tyr Asp Leu Leu Ser Asn Arg Val Ile Lys Lys Pro Met Ser 565 570 Ala Ser Ala Leu Phe Val Gln Asp His Arg Pro Gln Phe Leu Ile Glu 585 590 580 Asn Pro Lys Thr Ser Leu Glu Asp Ala Thr Leu Gln Ile Glu Glu Leu 595 600 Trp Lys Thr Leu Ser Glu Glu Glu Lys Leu Lys Tyr Glu Glu Lys Ala 615 620 Thr Lys Asp Leu Glu Arg Tyr Asn Ser Gln Met Lys Arg Ala Ile Glu 630 635 Gln Glu Ser Gln Met Ser Leu Lys Asp Gly Arg Lys Lys Ile Lys Pro 650 655 645 Thr Ser Ala Trp Asn Leu Ala Gln Lys His Lys Leu Lys Thr Ser Leu 665 Ser Asn Gln Pro Lvs Leu Asp Glu Leu Leu Gln Ser Gln Ile Glu Lys

675 680 685 Arg Arg Ser Gln Asn Ile Lys Met Val Gln Ile Pro Phe Ser Met Lys 695 700 Asn Leu Lys Ile Asn Phe Lys Lys Gln Asn Lys Val Asp Leu Glu Glu 710 715 Lys Asp Glu Pro Cys Leu Ile His Asn Leu Arg Phe Pro Asp Ala Trp 725 730 Leu Met Thr Ser Lys Thr Glu Val Met Leu Leu Asn Pro Tyr Arg Val 740 745 750 Glu Glu Ala Leu Leu Phe Lys Arg Leu Leu Glu Asn His Lys Leu Pro 760 765 Ala Glu Pro Leu Glu Lys Pro Ile Met Leu Thr Glu Ser Leu Phe Asn 770 775 780 Gly Ser His Tyr Leu Asp Val Leu Tyr Lys Met Thr Ala Asp Asp Gln 790 795 Arg Tyr Ser Gly Ser Thr Tyr Leu Ser Asp Pro Arg Leu Thr Ala Asn 810 815 805 Glv Phe Lys Ile Lys Leu Ile Pro Gly Val Ser Ile Thr Glu Asn Tyr 825 Leu Glu Ile Glu Gly Met Ala Asn Cys Leu Pro Phe Tyr Gly Val Ala 840 845 Asp Leu Lys Glu Ile Leu Asn Ala Ile Leu Asn Arg Asn Ala Lys Glu 855 860 Val Tyr Glu Cys Arg Pro Arg Lys Val Ile Ser Tyr Leu Glu Gly Glu 870 875 Ala Val Arg Leu Ser Arg Gln Leu Pro Met Tyr Leu Ser Lys Glu Asp 890 8.85 Ile Gln Asp Ile Ile Tyr Arg Met Lys His Gln Phe Gly Asn Glu Ile 905 Lys Glu Cys Val His Gly Arg Pro Phe Phe His His Leu Thr Tyr Leu 915 920 Pro Glu Thr Thr 930

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<213> Homo sapiens

### <400> 18

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Thr Lys Asp Leu Glu Arg Tyr Asn Ser Gln Met Lys Arg Ala Ile Glu 635 630 Gln Glu Ser Gln Met Ser Leu Lys Asp Gly Arg Lys Lys Ile Lys Pro 650 645 Thr Ser Ala Trp Asn Leu Ala Gln Lys His Lys Leu Lys Thr Ser Leu 660 665 Ser Asn Gln Pro Lys Leu Asp Glu Leu Leu Gln Ser Gln Ile Glu Lys 685 680 Arg Arg Ser Gln Asn Ile Lys Met Val Gln Ile Pro Phe Ser Met Lys 700 695 Asn Leu Lys Ile Asn Phe Lys Lys Gln Asn Lys Val Asp Leu Glu Glu 710 715 Lys Asp Glu Pro Cys Leu Ile His Asn Leu Arg Phe Pro Asp Ala Trp 725 730 735 Leu Met Thr Ser Lys Thr Glu Val Met Leu Leu Asn Pro Tyr Arg Val 745 750 Glu Glu Ala Leu Leu Phe Lys Arg Leu Leu Glu Asn His Lys Leu Pro 760 765 Ala Glu Pro Leu Glu Lys Pro Ile Met Leu Thr Glu Ser Leu Phe Asn 775 780 Gly Ser His Tyr Leu Asp Val Leu Tyr Lys Met Thr Ala Asp Asp Gln 790 795 Arg Tyr Ser Gly Ser Thr Tyr Leu Ser Asp Pro Arg Leu Thr Ala Asn 810 815 805 Gly Phe Lys Ile Lys Leu Ile Pro Gly Val Ser Ile Thr Glu Asn Tyr 825 830 Leu Glu Ile Glu Gly Met Ala Asn Cys Leu Pro Phe Tyr Gly Val Ala 840 845 Asp Leu Lys Glu Ile Leu Asn Ala Ile Leu Asn Arg Asn Ala Lys Glu 855 860 Val Tyr Glu Cys Arg Pro Arg Lys Val Ile Ser Tyr Leu Glu Gly Glu 875 870 Ala Val Arg Leu Ser Arg Gln Leu Pro Met Tyr Leu Ser Lys Glu Asp 885 890 895 Ile Gln Asp Ile Ile Tyr Arg Met Lys His Gln Phe Gly Asn Glu Ile 905 910 Lys Glu Cys Val His Gly Arg Pro Phe Phe His His Leu Thr Tyr Leu 915 920 Pro Glu Thr Thr

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930

<212> PRT <213> Homo sapiens

<400> 19

Gln Tyr Arg Val Glu Val Tyr Lys Asn Arg Ala Gly Asn Lys Ala Ser 105 Lys Glu Asn Asp Trp Tyr Leu Ala Tyr Lys Ala Ser Pro Gly Asn Leu 115 120 125 Ser Gln Phe Glu Asp Ile Leu Phe Gly Asn Asn Asp Met Ser Ala Ser 135 140 Ile Gly Val Val Gly Val Lys Met Ser Ala Val Asp Gly Gln Arg Gln 150 155 Val Gly Val Gly Tyr Val Asp Ser Ile Gln Arg Lys Leu Gly Leu Cys 165 170 Glu Phe Pro Asp Asn Asp Gln Phe Ser Asn Leu Glu Ala Leu Leu Ile 180 185 Gln Ile Gly Pro Lys Glu Cys Val Leu Pro Gly Gly Glu Thr Ala Gly 195 200 Asp Met Gly Lys Leu Arg Gln Ile Ile Gln Arg Gly Gly Ile Leu Ile 215 220 Thr Glu Arg Lys Lys Ala Asp Phe Ser Thr Lys Asp Ile Tyr Gln Asp 230 235 Leu Asn Arg Leu Leu Lys Gly Lys Lys Gly Glu Gln Met Asn Ser Ala 245 250 255 Val Leu Pro Glu Met Glu Asn Gln Val Ala Val Ser Ser Leu Ser Ala 260 265 270 Val Ile Lys Phe Leu Glu Leu Leu Ser Asp Asp Ser Asn Phe Gly Gln 275 280 285 Phe Glu Leu Thr Thr Phe Asp Phe Ser Gln Tyr Met Lys Leu Asp Ile 290 295 300 Ala Ala Val Arg Ala Leu Asn Leu Phe Gln Gly Ser Val Glu Asp Thr 310 315 Thr Gly Ser Gln Ser Leu Ala Ala Leu Leu Asn Lys Cys Lys Thr Pro 325 330 335 Gln Gly Gln Arg Leu Val Asn Gln Trp Ile Lys Gln Pro Leu Met Asp 340 345 350 Lys Asn Arg Ile Glu Glu Arg Leu Asn Leu Val Glu Ala Phe Val Glu 355 360 365 Asp Ala Glu Leu Arg Gln Thr Leu Gln Glu Asp Leu Leu Arg Arg Phe 370 375 380 Pro Asp Leu Asn Arg Leu Ala Lys Lys Phe Gln Arg Gln Ala Ala Asn 390 395 Leu Gln Asp Cys Tyr Arg Leu Tyr Gln Gly Ile Asn Gln Leu Pro Asn 405 410 415 Val Ile Gln Ala Leu Glu Lys His Glu Gly Lys His Gln Lys Leu Leu 420 425 430 Leu Ala Val Phe Val Thr Pro Leu Thr Asp Leu Arg Ser Asp Phe Ser 435 440 Lys Phe Gln Glu Met Ile Glu Thr Thr Leu Asp Met Asp Gln Val Glu 460 455 Asn His Glu Phe Leu Val Lys Pro Ser Phe Asp Pro Asn Leu Ser Glu 470 475 Leu Arg Glu Ile Met Asn Asp Leu Glu Lys Lys Met Gln Ser Thr Leu 485 490 Ile Ser Ala Ala Arg Asp Leu Gly Leu Asp Pro Gly Lys Gln Ile Lys 505 Leu Asp Ser Ser Ala Gln Phe Gly Tyr Tyr Phe Arg Val Thr Cys Lys 520 525 Glu Glu Lys Val Leu Arg Asn Asn Lys Asn Phe Ser Thr Val Asp Ile 535 540 Gln Lys Asn Gly Val Lys Phe Thr Asn Ser Lys Leu Thr Ser Leu Asn 555 550 Glu Glu Tyr Thr Lys Asn Lys Thr Glu Tyr Glu Glu Ala Gln Asp Ala

565 570 575 Ile Val Lys Glu Ile Val Asn Ile Ser Ser Gly Tyr Val Glu Pro Met 580 585 590 Gln Thr Leu Asn Asp Val Leu Ala Gln Leu Asp Ala Val Val Ser Phe 595 600 605 Ala His Val Ser Asn Gly Ala Pro Val Pro Tyr Val Arg Pro Ala Ile 615 620 Leu Glu Lys Gly Gln Gly Arg Ile Ile Leu Lys Ala Ser Arg His Ala 630 635 Cys Val Glu Val Gln Asp Glu Ile Ala Phe Ile Pro Asn Asp Val Tyr 645 650 655 Phe Glu Lys Asp Lys Gln Met Phe His Ile Ile Thr Gly Pro Asn Met 660 665 670 Gly Gly Lys Ser Thr Tyr Ile Arg Gln Thr Gly Val Ile Val Leu Met 675 680 685 Ala Gln Ile Gly Cys Phe Val Pro Cys Glu Ser Ala Glu Val Ser Ile 695 700 Val Asp Cys Ile Leu Ala Arg Val Gly Ala Gly Asp Ser Gln Leu Lys 715 720 705 710 Gly Val Ser Thr Phe Met Ala Glu Met Leu Glu Thr Ala Ser Ile Leu 725 730 735 Arg Ser Ala Thr Lys Asp Ser Leu Ile Ile Ile Asp Glu Leu Gly Arg 745 750 Gly Thr Ser Thr Tyr Asp Gly Phe Gly Leu Ala Trp Ala Ile Ser Glu 755 760 765 Tyr Ile Ala Thr Lys Ile Gly Ala Phe Cys Met Phe Ala Thr His Phe 775 780 His Glu Leu Thr Ala Leu Ala Asn Gln Ile Pro Thr Val Asn Asn Leu 790 795 800 His Val Thr Ala Leu Thr Thr Glu Glu Thr Leu Thr Met Leu Tyr Gln 810 815 805 Val Lys Lys Gly Val Cys Asp Gln Ser Phe Gly Ile His Val Ala Glu 820 825 830 Leu Ala Asn Phe Pro Lys His Val Ile Glu Cys Ala Lys Gln Lys Ala 835 840 845 Leu Glu Leu Glu Glu Phe Gln Tyr Ile Gly Glu Ser Gln Gly Tyr Asp 850 855 860 Ile Met Glu Pro Ala Ala Lys Lys Cys Tyr Leu Glu Arg Glu Gln Gly 870 875 Glu Lys Ile Ile Gln Glu Phe Leu Ser Lys Val Lys Gln Met Pro Phe 885 890 Thr Glu Met Ser Glu Glu Asn Ile Thr Ile Lys Leu Lys Gln Leu Lys 905 900 910 Ala Glu Val Ile Ala Lys Asn Asn Ser Phe Val Asn Glu Ile Ile Ser 915 920 Arg Ile Lys Val Thr Thr

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930

<213> Homo sapiens

<400> 20

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40 Val Ile Val Lys Glu Gly Gly Leu Lys Leu Ile Gln Ile Gln Asp Asn 55 60 Gly Thr Gly Ile Arg Lys Glu Asp Leu Asp Ile Val Cys Glu Arg Phe 70 75 Thr Thr Ser Lys Leu Gln Ser Phe Glu Asp Leu Ala Ser Ile Ser Thr 90 85 Tyr Gly Phe Arg Gly Glu Ala Leu Ala Ser Ile Ser His Val Ala His 100 1.05 Val Thr Ile Thr Thr Lys Thr Ala Asp Gly Lys Cys Ala Tyr Arg Ala 115 120 125 Ser Tyr Ser Asp Gly Lys Leu Lys Ala Pro Pro Lys Pro Cys Ala Gly 135 140 Asn Gln Gly Thr Gln Ile Thr Val Glu Asp Leu Phe Tyr Asn Ile Ala 150 155 Thr Arg Arg Lys Ala Leu Lys Asn Pro Ser Glu Glu Tyr Gly Lys Ile 165 170 Leu Glu Val Val Gly Arg Tyr Ser Val His Asn Ala Gly Ile Ser Phe 180 185 Ser Val Lys Lys Gln Gly Glu Thr Val Ala Asp Val Arg Thr Leu Pro 195 200 205 Asn Ala Ser Thr Val Asp Asn Ile Arg Ser Ile Phe Gly Asn Ala Val 220 215 Ser Arg Glu Leu Ile Glu Ile Gly Cys Glu Asp Lys Thr Leu Ala Phe 230 235 Lys Met Asn Gly Tyr Ile Ser Asn Ala Asn Tyr Ser Val Lys Lys Cys 245 250 Ile Phe Leu Leu Phe Ile Asn His Arg Leu Val Glu Ser Thr Ser Leu 260 265 270 Arg Lys Ala Ile Glu Thr Val Tyr Ala Ala Tyr Leu Pro Lys Asn Thr 275 280 285 His Pro Phe Leu Tyr Leu Ser Leu Glu Ile Ser Pro Gln Asn Val Asp 295 300 Val Asn Val His Pro Thr Lys His Glu Val His Phe Leu His Glu Glu 310 315 Ser Ile Leu Glu Arg Val Gln Gln His Ile Glu Ser Lys Leu Leu Gly 325 330 335 Ser Asn Ser Ser Arg Met Tyr Phe Thr Gln Thr Leu Leu Pro Gly Leu 340 345 350 Ala Gly Pro Ser Gly Glu Met Val Lys Ser Thr Thr Ser Leu Thr Ser 355 360 365 Ser Ser Thr Ser Gly Ser Ser Asp Lys Val Tyr Ala His Gln Met Val 375 380 Arg Thr Asp Ser Arg Glu Gln Lys Leu Asp Ala Phe Leu Gln Pro Leu 395 400 390 Ser Lys Pro Leu Ser Ser Gln Pro Gln Ala Ile Val Thr Glu Asp Lys 405 410 Thr Asp Ile Ser Ser Gly Arg Ala Arg Gln Gln Asp Glu Glu Met Leu 420 425 Glu Leu Pro Ala Pro Ala Glu Val Ala Ala Lys Asn Gln Ser Leu Glu 435 440 Gly Asp Thr Thr Lys Gly Thr Ser Glu Met Ser Glu Lys Arg Gly Pro 450 455 460 Thr Ser Ser Asn Pro Arg Lys Arg His Arg Glu Asp Ser Asp Val Glu 470 475 Met Val Glu Asp Asp Ser Arg Lys Glu Met Thr Ala Ala Cys Thr Pro 485 490 Arg Arg Arg Ile Ile Asn Leu Thr Ser Val Leu Ser Leu Gln Glu Glu 505 510

Ile Asn Glu Gln Gly His Glu Val Leu Arg Glu Met Leu His Asn His 520 515 Ser Phe Val Gly Cys Val Asn Pro Gln Trp Ala Leu Ala Gln His Gln 535 540 Thr Lys Leu Tyr Leu Leu Asn Thr Thr Lys Leu Ser Glu Glu Leu Phe 550 555 Tyr Gln Ile Leu Ile Tyr Asp Phe Ala Asn Phe Gly Val Leu Arg Leu 565 570 575 Ser Glu Pro Ala Pro Leu Phe Asp Leu Ala Met Leu Ala Leu Asp Ser 580 585 590 Pro Glu Ser Gly Trp Thr Glu Glu Asp Gly Pro Lys Glu Gly Leu Ala 595 600 605 Glu Tyr Ile Val Glu Phe Leu Lys Lys Lys Ala Glu Met Leu Ala Asp 615 620 Tyr Phe Ser Leu Glu Ile Asp Glu Glu Gly Asn Leu Ile Gly Leu Pro 630 635 Leu Leu Ile Asp Asn Tyr Val Pro Pro Leu Glu Gly Leu Pro Ile Phe 650 655 645 Ile Leu Arg Leu Ala Thr Glu Val Asn Trp Asp Glu Glu Lys Glu Cys 665 670 Phe Glu Ser Leu Ser Lys Glu Cys Ala Met Phe Tyr Ser Ile Arg Lys 680 685 Gln Tyr Ile Ser Glu Glu Ser Thr Leu Ser Gly Gln Gln Ser Glu Val 695 700 Pro Gly Ser Ile Pro Asn Ser Trp Lys Trp Thr Val Glu His Ile Val 710 715 Tyr Lys Ala Leu Arg Ser His Ile Leu Pro Pro Lys His Phe Thr Glu 725 730 735 Asp Gly Asn Ile Leu Gln Leu Ala Asn Leu Pro Asp Leu Tyr Lys Val 740 745 Phe Glu Arg Cys

755
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<211> 133
<212> PRT

<213> Homo sapiens

<400> 21

Met Lys Gln Leu Pro Ala Ala Thr Val Arg Leu Leu Ser Ser Ser Gln 10 Ile Ile Thr Ser Val Val Ser Val Val Lys Glu Leu Ile Glu Asn Ser 20 25 Leu Asp Ala Gly Ala Thr Ser Val Asp Val Lys Leu Glu Asn Tyr Gly 40 Phe Asp Lys Ile Glu Val Arg Asp Asn Gly Glu Gly Ile Lys Ala Val 55 Asp Ala Pro Val Met Ala Met Lys Tyr Tyr Thr Ser Lys Ile Asn Ser 70 75 His Glu Asp Leu Glu Asn Leu Thr Thr Tyr Gly Phe Arg Gly Glu Ala 85 90 Leu Gly Ser Ile Cys Cys Ile Ala Glu Val Leu Ile Thr Thr Arg Thr 105 Ala Ala Asp Asn Phe Ser Thr Gln Tyr Val Leu Asp Gly Ser Gly His 115 120 Ile Leu Ser Gln Lys

130

<211> 1360

<212> PRT <213> Homo sapiens

<400> 22

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425

430

Tyr Glu Leu Tyr His Met Asp Ala Leu Ile Gly Val Ser Glu Leu Gly 440 Leu Val Phe Met Lys Gly Asn Trp Ala His Ser Gly Phe Pro Glu Ile 455 460 Ala Phe Gly Arg Tyr Ser Asp Ser Leu Val Gln Lys Gly Tyr Lys Val 475 470 Ala Arg Val Glu Gln Thr Glu Thr Pro Glu Met Met Glu Ala Arg Cys 490 485 Arg Lys Met Ala His Ile Ser Lys Tyr Asp Arg Val Val Arg Arg Glu 505 Ile Cys Arg Ile Ile Thr Lys Gly Thr Gln Thr Tyr Ser Val Leu Glu 520 Gly Asp Pro Ser Glu Asn Tyr Ser Lys Tyr Leu Leu Ser Leu Lys Glu 535 540 Lys Glu Glu Asp Ser Ser Gly His Thr Arg Ala Tyr Gly Val Cys Phe 550 555 Val Asp Thr Ser Leu Gly Lys Phe Phe Ile Gly Gln Phe Ser Asp Asp 570 565 Arg His Cys Ser Arg Phe Arg Thr Leu Val Ala His Tyr Pro Pro Val 585 Gln Val Leu Phe Glu Lys Gly Asn Leu Ser Lys Glu Thr Lys Thr Ile 600 605 Leu Lys Ser Ser Leu Ser Cys Ser Leu Gln Glu Gly Leu Ile Pro Gly 615 620 Ser Gln Phe Trp Asp Ala Ser Lys Thr Leu Arg Thr Leu Leu Glu Glu 630 635 Glu Tyr Phe Arg Glu Lys Leu Ser Asp Gly Ile Gly Val Met Leu Pro 650 645 Gln Val Leu Lys Gly Met Thr Ser Glu Ser Asp Ser Ile Gly Leu Thr 665 660 Pro Gly Glu Lys Ser Glu Leu Ala Leu Ser Ala Leu Gly Gly Cys Val 680 685 Phe Tyr Leu Lys Lys Cys Leu Ile Asp Gln Glu Leu Leu Ser Met Ala 700 695 Asn Phe Glu Glu Tyr Ile Pro Leu Asp Ser Asp Thr Val Ser Thr Thr 715 710 Arg Ser Gly Ala Ile Phe Thr Lys Ala Tyr Gln Arg Met Val Leu Asp 725 730 Ala Val Thr Leu Asn Asn Leu Glu Ile Phe Leu Asn Gly Thr Asn Gly 740 745 Ser Thr Glu Gly Thr Leu Leu Glu Arg Val Asp Thr Cys His Thr Pro 760 765 Phe Gly Lys Arg Leu Leu Lys Gln Trp Leu Cys Ala Pro Leu Cys Asn 775 780 His Tyr Ala Ile Asn Asp Arg Leu Asp Ala Ile Glu Asp Leu Met Val 795 790 Val Pro Asp Lys Ile Ser Glu Val Val Glu Leu Leu Lys Lys Leu Pro 805 810 Asp Leu Glu Arg Leu Leu Ser Lys Ile His Asn Val Gly Ser Pro Leu 825 820 Lys Ser Gln Asn His Pro Asp Ser Arg Ala Ile Met Tyr Glu Glu Thr 840 835 Thr Tyr Ser Lys Lys Lys Ile Ile Asp Phe Leu Ser Ala Leu Glu Gly 855 860 Phe Lys Val Met Cys Lys Ile Ile Gly Ile Met Glu Glu Val Ala Asp 875 870 Gly Phe Lys Ser Lys Ile Leu Lys Gln Val Ile Ser Leu Gln Thr Lys 890 885 Asn Pro Glu Gly Arg Phe Pro Asp Leu Thr Val Glu Leu Asn Arg Trp

905 900 Asp Thr Ala Phe Asp His Glu Lys Ala Arg Lys Thr Gly Leu Ile Thr 915 920 925 Pro Lys Ala Gly Phe Asp Ser Asp Tyr Asp Gln Ala Leu Ala Asp Ile 930 935 940 Arg Glu Asn Glu Gln Ser Leu Leu Glu Tyr Leu Glu Lys Gln Arg Asn 950 955 Arg Ile Gly Cys Arg Thr Ile Val Tyr Trp Gly Ile Gly Arg Asn Arg 965 970 975 Tyr Gln Leu Glu Ile Pro Glu Asn Phe Thr Thr Arg Asn Leu Pro Glu 980 985 990 Glu Tyr Glu Leu Lys Ser Thr Lys Lys Gly Cys Lys Arg Tyr Trp Thr 995 1000 1005 Lys Thr Ile Glu Lys Lys Leu Ala Asn Leu Ile Asn Ala Glu Glu Arg 1010 1015 1020 Arg Asp Val Ser Leu Lys Asp Cys Met Arg Arg Leu Phe Tyr Asn Phe 1025 1030 1035 1040 Asp Lys Asn Tyr Lys Asp Trp Gln Ser Ala Val Glu Cys Ile Ala Val 1045 1050 1055 Leu Asp Val Leu Leu Cys Leu Ala Asn Tyr Ser Arg Gly Gly Asp Gly 1060 1065 1070 Pro Met Cys Arg Pro Val Ile Leu Leu Pro Glu Asp Thr Pro Pro Phe 1075 1080 1085 Leu Glu Leu Lys Gly Ser Arg His Pro Cys Ile Thr Lys Thr Phe Phe 1090 1095 1100 Gly Asp Asp Phe Ile Pro Asn Asp Ile Leu Ile Gly Cys Glu Glu Glu 1105 1110 1115 Glu Gln Glu Asn Gly Lys Ala Tyr Cys Val Leu Val Thr Gly Pro Asn 1125 1130 1135 Met Gly Gly Lys Ser Thr Leu Met Arg Gln Ala Gly Leu Leu Ala Val 1140 1145 1150 Met Ala Gln Met Gly Cys Tyr Val Pro Ala Glu Val Cys Arg Leu Thr 1155 1160 1165 Pro Ile Asp Arg Val Phe Thr Arg Leu Gly Ala Ser Asp Arg Ile Met 1170 1175 1180 Ser Gly Glu Ser Thr Phe Phe Val Glu Leu Ser Glu Thr Ala Ser Ile 1185 1190 1195 1200 Leu Met His Ala Thr Ala His Ser Leu Val Leu Val Asp Glu Leu Gly 1205 1210 1215 Arg Gly Thr Ala Thr Phe Asp Gly Thr Ala Ile Ala Asn Ala Val Val 1220 1225 1230 Lys Glu Leu Ala Glu Thr Ile Lys Cys Arg Thr Leu Phe Ser Thr His 1235 1240 1245 Tyr His Ser Leu Val Glu Asp Tyr Ser Gln Asn Val Ala Val Arg Leu 1250 1255 1260 Gly His Met Ala Cys Met Val Glu Asn Glu Cys Glu Asp Pro Ser Gln 1265 1270 1275 1280 Glu Thr Ile Thr Phe Leu Tyr Lys Phe Ile Lys Gly Ala Cys Pro Lys 1285 1290 Ser Tyr Gly Phe Asn Ala Ala Arg Leu Ala Asn Leu Pro Glu Glu Val 1300 1305 1310 Ile Gln Lys Gly His Arg Lys Ala Arg Glu Phe Glu Lys Met Asn Gln 1315 1320 1325 Ser Leu Arg Leu Phe Arg Glu Val Cys Leu Ala Ser Glu Arg Ser Thr 1335 1340 Val Asp Ala Glu Ala Val His Lys Leu Leu Thr Leu Ile Lys Glu Leu 1350 1355

<211> 389 <212> PRT

<213> Homo sapiens

<400> 23 Met Ala Gln Pro Lys Gln Glu Arg Val Ala Arg Ala Arg His Gln Arg 10 Ser Glu Thr Ala Arg His Gln Arg Ser Glu Thr Ala Lys Thr Pro Thr 2.5 Leu Gly Asn Arg Gln Thr Pro Thr Leu Gly Asn Arg Gln Thr Pro Arg 40 Leu Gly Ile His Ala Arg Pro Arg Arg Arg Ala Thr Thr Ser Leu Leu 55 Thr Leu Leu Leu Ala Phe Gly Lys Asn Ala Val Arg Cys Ala Leu Ile 70 75 Gly Pro Gly Ser Leu Thr Ser Arg Thr Arg Pro Leu Thr Glu Pro Leu 90 85 Gly Glu Lys Glu Arg Arg Glu Val Phe Phe Pro Pro Arg Pro Glu Arg 100 105 110 Val Glu His Asn Val Glu Ser Ser Arg Trp Glu Pro Arg Arg Arg Gly 115 120 125 Ala Cys Gly Ser Arg Gly Gly Asn Phe Pro Ser Pro Arg Gly Gly Ser 135 140 130 Gly Val Ala Ser Leu Glu Arg Ala Glu Asn Ser Ser Thr Glu Pro Ala 145 150 155 Lys Ala Ile Lys Pro Ile Asp Arg Lys Ser Val His Gln Ile Cys Ser 165 170 175 Gly Pro Val Val Pro Ser Leu Arg Pro Asn Ala Val Lys Glu Leu Val 180 185 190 Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn Val Asp Leu Lys Leu Lys 195 200 205 Asp Tyr Gly Val Asp Leu Ile Glu Val Ser Gly Asn Gly Cys Gly Val 210 215 220 Glu Glu Glu Asn Phe Glu Gly Phe Thr Leu Lys His His Thr Cys Lys 225 230 235 Ile Gln Glu Phe Ala Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg 245 - 250 Gly Glu Ala Leu Ser Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser 260 265 270 Thr Cys Arg Val Ser Ala Lys Val Gly Thr Arg Leu Val Phe Asp His 275 280 285 Tyr Gly Lys Ile Ile Gln Lys Thr Pro Tyr Pro Arg Pro Arg Gly Met 290 295 300 Thr Val Ser Val Lys Gln Leu Phe Ser Thr Leu Pro Val His His Lys 310 315 Glu Phe Gln Arg Asn Ile Lys Lys Lys Arg Ala Cys Phe Pro Phe Ala 325 330 335 Phe Cys Arg Asp Cys Gln Phe Pro Glu Ala Ser Pro Ala Met Leu Pro 340 345 Val Gln Pro Val Glu Leu Thr Pro Arg Ser Thr Pro Pro His Pro Cys 360 365 355 Ser Leu Glu Asp Asn Val Ile Thr Val Phe Ser Ser Val Lys Asn Gly 380 375 Pro Gly Ser Ser Arg

<210> 24 <211> 264

<212> PRT

### <213> Homo sapiens

<400> 24 Met Cys Pro Trp Arg Pro Arg Leu Gly Arg Arg Cys Met Val Ser Pro 10 Arg Glu Ala Asp Leu Gly Pro Gln Lys Asp Thr Arg Leu Asp Leu Pro Arg Ser Pro Ala Arg Ala Pro Arg Glu Gln Asn Ser Leu Gly Glu Val 40 Asp Arg Arg Gly Pro Arg Glu Gln Thr Arg Ala Pro Ala Thr Ala Ala 55 Pro Pro Arg Pro Leu Gly Ser Arg Gly Ala Glu Ala Ala Glu Pro Gln 7.0 75 Glu Gly Leu Ser Ala Thr Val Ser Ala Cys Phe Gln Glu Gln Gln Glu 85 90 Met Asn Thr Leu Gln Gly Pro Val Ser Phe Lys Asp Val Ala Val Asp 100 105 Phe Thr Gln Glu Glu Trp Arg Gln Leu Asp Pro Asp Glu Lys Ile Ala 120 125 Tyr Gly Asp Val Met Leu Glu Asn Tyr Ser His Leu Val Ser Val Gly 135 Tyr Asp Tyr His Gln Ala Lys His His Gly Val Glu Val Lys Glu 150 155 Val Glu Gln Gly Glu Glu Pro Trp Ile Met Glu Gly Glu Phe Pro Cys 170 165 Gln His Ser Pro Glu Pro Ala Lys Ala Ile Lys Pro Ile Asp Arg Lys 185 Ser Val His Gln Ile Cys Ser Gly Pro Val Val Leu Ser Leu Ser Thr 200 205 Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn 210 215 220 Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp Leu Ile Glu Val Ser 230 235 Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe Glu Gly Leu Ile Ser 245 250 Phe Ser Ser Glu Thr Ser His Met

<210> 25 <211> 264 <212> PRT

260

<213> Homo sapiens

<400> 25

Met Cys Pro Trp Arg Pro Arg Leu Gly Arg Arg Cys Met Val Ser Pro 10 Arg Glu Ala Asp Leu Gly Pro Gln Lys Asp Thr Arg Leu Asp Leu Pro 20 25 3.0 Arg Ser Pro Ala Arg Ala Pro Arg Glu Gln Asn Ser Leu Gly Glu Val 40 45 Asp Arg Arg Gly Pro Arg Glu Gln Thr Arg Ala Pro Ala Thr Ala Ala 55 60 Pro Pro Arg Pro Leu Gly Ser Arg Gly Ala Glu Ala Ala Glu Pro Gln 70 75 Glu Gly Leu Ser Ala Thr Val Ser Ala Cys Phe Gln Glu Gln Glu 90 Met Asn Thr Leu Gln Gly Pro Val Ser Phe Lys Asp Val Ala Val Asp 105 Phe Thr Gln Glu Glu Trp Arg Gln Leu Asp Pro Asp Glu Lys Ile Ala

125 120 115 Tyr Gly Asp Val Met Leu Glu Asn Tyr Ser His Leu Val Ser Val Gly 130 135 140 Tyr Asp Tyr His Gln Ala Lys His His His Gly Val Glu Val Lys Glu 150 155 Val Glu Gln Gly Glu Glu Pro Trp Ile Met Glu Gly Glu Phe Pro Cys 165 170 175 Gln His Ser Pro Glu Pro Ala Lys Ala Ile Lys Pro Ile Asp Arg Lys 180 185 190 Ser Val His Gln Ile Cys Ser Gly Pro Val Val Leu Ser Leu Ser Thr 195 200 205 Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp Ala Gly Ala Thr Asn 210 215 220 Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp Leu Ile Glu Val Ser 225 230 235 Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe Glu Gly Leu Ile Ser 245 250 Phe Ser Ser Glu Thr Ser His Met . 260

<210> 26

<400> 26